SYNTHESIS OF BENZIMIDAZOLE DERIVATIVES

VI.* N-HETARYLBENZIMIDAZOLES

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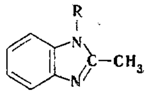
UDC 547.785.5.07: 541.651

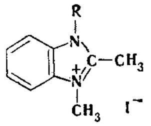
In an aqueous medium, the reaction of N-sodio-2-methylbenzimidazole with monohalogen-substituted nitrogenous aromatic heterocycles containing the halogen in the α position to the nitrogen atom may be considered as a method for obtaining N-betaryl-2-methylbenzimidazoles. 1-(Benzoxazol-2-yl)- and 1-(benzothiazol-2-yl)-2-methylbenzimidazoles have been synthesized; imidacyanine dyes have been obtained with benzothiazol-2-yl groups on the nitrogen atoms of the benzimidazole nuclei from the methiodide of the latter.

Of the N-hetarylbenzimidazoles and their salts, only compounds containing pyridine [1-3] and benzimidazole [4, 5] residues are known. Some of these compounds have been obtained by direct hetarylation – for example, benzimidazolylbenzimidazolium salts by heating benzimidazole with 2-chlorobenzimidazole or with 2-chloro-1-methylbenzimidazole [5].

It appeared of interest to synthesize 2-methylbenzimidazoles with other electrophilic hetaryl substituents on the 1-nitrogen atom of the imidazole ring and to determine the possibility of obtaining quaternary salts from them, and imidacyanines from these salts. For this purpose, for the hetarylation of 2-methylbenzimidazole we have used 2-chlorobenzoxazole and 2-chlorobenzothiazole, which were caused to react with N-sodio-2-methylbenzimidazole, prepared by a method [6] now somewhat modified for performance in dimethylformamide. The brief heating of 2-chlorobenzoxazole or 2-chlorobenzothiazole with a solution of N-sodio-2-methylbenzimidazole in dimethylformamide gave good yields of 1-(benzoxazol-2-yl)- and 1-(benzothiazol-2-yl)-2-methylbenzimidazoles (I and II).

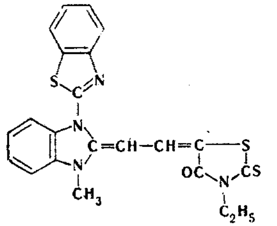


I, II

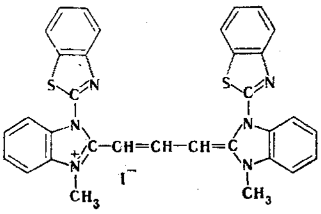


III, IV

I, III R = benzoxazol-2-yl; II, IV R = benzothiazolyl



V



VI

On being heated with an excess of methyl iodide, the bases (I) and (II) reacted as monoacid bases: only the N_3 atom of the benzimidazole nucleus took part in salt formation, with the production of the methiodides (III) and (IV). These salts are extremely unstable and decompose on heating and at least partially in some

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* For Communication V, see [1].

Institute of Organic Chemistry, Academy of Sciences of the Ukrainian SSR, Kiev. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 11, pp. 1542-1544, November, 1973. Original article submitted July 15, 1972.

chemical reactions; thus, it was impossible to obtain imidacyanine dyes from the salt (III), and from the salt (IV) they were obtained only with the accurate observance of the selected conditions and in low yields (V and VI).

From a comparison of the colors of the dye (VI) (λ_{max} 518) with that of known imidacarbocyanines – 1,1',3,3'-tetramethylimidacarbocyanine iodide (λ_{max} 491 nm) and 3,3'-dimethyl-1,1'-diphenylimidacarbocyanine iodide (λ_{max} 504 nm) [7] – it follows that in the symmetrical imidacarbocyanines the replacement of the alkyl groups present on the nitrogen atoms of the benzimidazole nuclei by aryl groups and then by hetaryl groups leads to a successive deepening of the color: the replacement of one methyl group by a phenyl group causes a long-wave shift of the absorption maximum by 6.5 nm, the replacement of a phenyl group by a benzothiazol-2-yl group a shift by 7 nm, and the replacement of a methyl group by a benzothiazol-2-yl group a shift by 14 nm.

EXPERIMENTAL

The main absorption maxima of the dyes (λ_{max}) were determined on an SF-10 spectrophotometer in ethanol.

N-Sodio-2-methylbenzimidazole. To a hot solution of 1.32 g (0.01 mole) of 2-methylbenzimidazole in 10 ml of anhydrous xylene was added 0.23 g (0.01 g-atom) of sodium in one portion, and the mixture was heated until a vigorous reaction set in with the sodium being converted into a gray suspension; heating was stopped to slow down the reaction, and then the whitish suspension was boiled for 2 h. The white precipitate of the N-sodium derivative was rapidly filtered off and washed on the filter with dry xylene and petroleum ether, and it was immediately dissolved in 10 ml of purified and dehydrated dimethylformamide, after which the solution was filtered from residues of sodium and was used for the synthesis of the N-hetaryl-2-methylbenzimidazoles.

1-(Benzoxazol-2-yl)-2-methylbenzimidazole (I). To a solution of N-sodio-2-methylbenzimidazole in dimethylformamide was added 1.54 g (0.01 mole) of 2-chlorobenzoxazole, and the mixture, the temperature of which had risen spontaneously, was boiled for 40 min. Then the dimethylformamide was distilled off completely in vacuum. The solid residue was extracted with petroleum ether and the solution was then mixed with 200 ml of boiled water. Then it was filtered off again, washed with water, and dried. Small white needles with mp 145°C. Yield 2.2 g (88.3%). Found: N 17.1%. $C_{15}H_{11}N_3O$. Calculated: N 16.9%.

1-(Benzoxazol-2-yl)-2,3-dimethylbenzimidazolium Iodide (III). A mixture of 0.25 g (0.001 mole) of the base (I) and 2 ml of methyl iodide was heated in a sealed glass tube at 115-125°C for 2 h. The mixture was treated with acetone and filtered, and the residue was washed with acetone. Yield almost quantitative. The substance was crystallized from 25 ml of ethanol (using carbon) and was washed with ethanol and ether. Lustrous colorless plates with mp 240°C (decomp.). Found: I 32.8%. $C_{16}H_{14}IN_3O$. Calculated: I 32.5%.

1-(Benzothiazol-2-yl)-2-methylbenzimidazole (II). To a solution of N-sodio-2-methylbenzimidazole was added 1.7 g (0.01 mole) of 2-chlorbenzothiazole, and the mixture was boiled for 45 min. The precipitate of sodium chloride was filtered off and everything boiling at a residual pressure of 2 mm on heating in a bath, the temperature of which was raised during distillation from 30 to 70°C, was distilled off. The crystallized residue was washed by decantation with petroleum ether, treated with 25 ml of 20% caustic soda heated to 60°C, washed with water, and dried in the air. Then it was extracted three times with hot heptane (30, 10, and 10 ml), the extract was decolorized with carbon and it was left for 3 h; the product was washed with petroleum ether. Yield 1.5 g (56.5%). Colorless crystals with mp 80-82°C. Found: N 16.0; S 12.1%. $C_{15}H_{11}N_3S$. Calculated: N 15.8; S 12.1%.

1-(Benzothiazol-2-yl)-2,3-dimethylbenzimidazolium Iodide (IV). This was obtained in a similar manner to the methiodide of the base (I), but in this case the time of heating was 1 h at 100°C. Yield almost quantitative. It was crystallized from 180-190 ml of ethanol. Colorless crystals with a mother-of-pearl luster, mp 269-270°C (decomp.). Found: I 31.0%. $C_{16}H_{14}IN_3S$. Calculated: I 31.2%.

5-{2-[1-(Benzothiazol-2-yl)-3-methylbenzimidazolin-2-ylidene]ethylidene}-3-ethyl-2-thioxothiazolidin-4-one (V). A mixture of 1.0 g (2.46 mmoles) of the methiodide (IV), 0.67 g (2.25 mmoles) of 5-(acetanilidomethylene)-3-ethylrhodanine, 5 ml of anhydrous pyridine, and 0.4 g of triethylamine was heated to the boil, and the resulting solution was heated in the boiling water bath for 50 min. Then 30 ml of ethanol was added and the mixture was left for 1 h. The precipitate of dye was washed with ether and dissolved in 4 ml of pyridine, the solution was treated with 4 ml of ethanol, and, after 2 h, long acicular red crystals of the dye (V) with a slight bluish tinge were filtered off; mp 206-208°C, λ_{max} 521 nm. Yield 0.05 g (5%). Found: N 12.4; S 21.1%. $C_{22}H_{18}N_4OS_3$. Calculated: N 12.4; S 21.3%.

On standing for 2-3 days, the alcoholic pyridine mother solution from which the dye (V) had been filtered off deposited a small amount of yellow crystals which were not investigated; this substance – obviously a decomposition product of the dye – is formed in large amount if the preparation of the dye is performed under more severe conditions.

1,1'-Di(benzothiazol-2-yl)-3,3'-dimethylimidacarbocyanine Iodide (VI). A solution of 0.88 g (0.006 mole) of diethoxymethyl acetate [8] in 2 ml of nitrobenzene was added to a hot suspension of 0.81 g (0.002 mole) of the methiodide (IV) in 13 ml of nitrobenzene, and the mixture was rapidly heated to 120°C, after which it was heated for another 1 h on the boiling-water bath. Then it was poured into 100 ml of ether and the dye was filtered off and was washed repeatedly with ether and 4-5 times by decantation with hot water, being carefully triturated with it; it was kept under water until it solidified. Then it was ground, washed with water, and dissolved in 7 ml of pyridine, and the solution was filtered and was poured into a hot solution of 0.5 g of sodium iodide in 35 ml of ethanol. After 3-4 h, the precipitate of the dye was washed with water and with ether. Yield 0.15 g (21.5%). Dark red crystals with a greenish metallic luster, mp 210°C (decomp.). Found: I 17.9%. $C_{33}H_{25}IN_6S_2$. Calculated: I 18.2%. λ_{max} 518 nm. Under UV light, an ethanolic solution of the dye has an intense orange fluorescence.

LITERATURE CITED

1. V. M. Zubarovskii and S. V. Lepikhova, Khim. Geterotsikl. Soedin., 687 (1972).
2. M. Gandino, P. Merli, and O. Turilli, French Patent No. 1,491,399 (1967); Chem. Abstr., 68, 11167 (1968).
3. M. Gandino, P. Merli, and O. Turilli, US Patent No. 3,443,955 (1969); Chem. Abstr., 71, 107 (1969).
4. A. M. Simonov and S. N. Kolodyazhnaya, Khim. Geterotsikl. Soedin., Collection 1 [in Russian] (1967), p. 141.
5. S. N. Kolodyazhnaya, A. M. Simonov, Yu. V. Kolodyazhnyi, O. A. Osipov, V. A. Bren', and I. D. Sadekov Khim. Geterotsikl. Soedin., 238 (1970).
6. V. M. Zubarovskii and G. P. Khodot, Khim. Geterotsikl. Soedin., 1559 (1970).
7. A. Van Dormael, Science et Industries Photographique, 20, 451 (1949).
8. H. Post and E. Erikson, J. Org. Chem., 2, 263 (1937).